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Case Report

Term pregnancy after the diagnosis of benign metastasizing leiomyomatosis

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Abstract
Benign metastasizing leiomyomatosis (BML) is a rare entity characterized by extrauterine tumoral formation of smooth muscle cells with histologic, immunologic, and molecular features similar to uterine leiomyomas. The most common site of metastasis is the lungs, but they can spread to any site in the body. A 30-year old woman with a history of myomectomy presented with symptoms of low back pain. A Tru-cut biopsy of the 50×40-mm solid mass in the right paraspinal muscle detected on magnetic resonance imaging was diagnosed as BML, and the mass was surgically resected. A 17-mm solid nodule was detected in the upper lobe of the right lung on chest computed tomography. The patient became pregnant one year after the diagnosis. An uneventful pregnancy resulted in a live birth at 38 weeks of gestation. BML may have different clinical presentations and progression patterns, and aggressive treatments can be avoided with an individual approach.

Keywords
Benign Metastasizing Leiomyomatosis, Myomectomy, Pregnancy

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Introduction

Benign Metastasizing Leiomyoma (BML) is a rare tumoral formation of smooth muscle cells without malignant features located in any tissue in the body. Although the most frequent sites of metastasis are the lungs (79.5%), the abdominal cavity, retroperitoneum, muscular tissue, bone, lymph node, blood vessels or even heart have also been reported to be affected [1]. Albeit explanations for its etiology do not go beyond theories, it mostly occurs years after myomectomy or hysterectomy performed for leiomyoma. In the review containing the largest number of patients on the subject, it was reported that the mean age at the time of the first surgery was 38.5 years, the mean age of diagnosis was 47.3 years, and the average interval between the first surgery and diagnosis was 8.8 years [2]. Due to the rarity of this disease, treatment has not been standardized. Suppression of estrogen production has been the main goal in treatment [1]. Our case is unique; the diagnosis of BML was made at a young age, shortly after the patient underwent uterine surgery, and despite the increased endogenous estrogen, the pregnancy after diagnosis was uneventful and resulted in a live birth.

Case Report

A 30-year-old woman with a history of two vaginal deliveries and a myomectomy one year ago presented to the clinic with symptoms of low back pain and a palpable mass on the right side of the spine, at the waist level. Magnetic resonance imaging (MRI) revealed the presence of a 50×40-mm mass located in the right paraspinal muscle at the L3-L4 level (Figure 1). A Tru-cut biopsy was performed with the preliminary diagnosis of schwannoma. A mesenchymal tumor, which demonstrated immunohistochemically to be positive for desmin, vimentin, smooth muscle actin (SMA), and estrogen/progesterone receptors (ER,PR), and negative for S-100 and a low tumor cell proliferation index (Ki67 index of 0-1%) was defined as leiomyoma. The low mitosis index, no evidence of anaplasia or necrosis, and minimal vascularization differentiated the lesion from leiomyosarcoma. Transvaginal ultrasound and MRI showed 25-mm type 3 and 19-mm type 4 fibroids in the uterus, and chest computed tomography (CT) revealed a 17x12-mm nodule in the upper lobe of the right lung (Figure 2). Positron emission tomography/computed tomography (PET-CT) scan showed no additional focus of metastasis except the existing lesions. The tumor in the paraspinal muscle was surgically resected (Figure 3). The patient, who could not tolerate estrogen suppression treatment with gonadotropin-releasing hormone analogs (GnRHa), became pregnant one year after the diagnosis. An uneventful pregnancy without BML-related symptoms or significant progression of the existing lesions resulted in a live birth by elective cesarean section at 38 weeks of gestation. During cesarean section, no contour irregularity and fibroids were observed on the outer surface of the uterus. In the postpartum 2nd-month transvaginal ultrasound evaluation, it was determined that the number and size of uterine myomas were constant. A chest CT scan showed that the pulmonary lesion of the patient, without any clinical pulmonary symptoms, had progressed to 27×16 mm, and there was no metastatic residual lesion in the MRI of the paraspinal lumbar muscle from

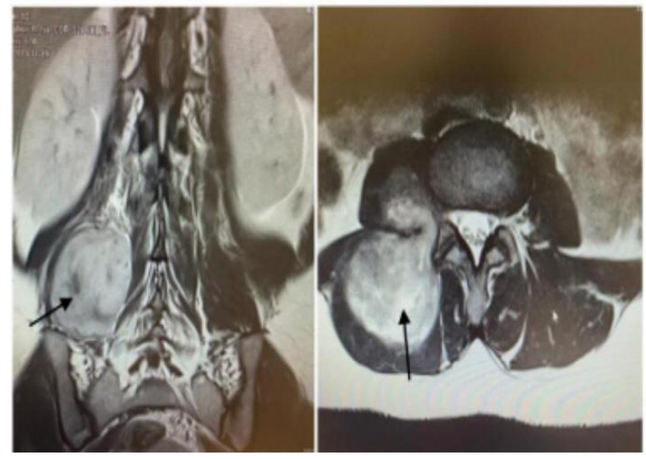

Figure 1. Well-demarcated isointense mass lesion located in the right paraspinal muscle on coronal and axial T2-weighted Magnetic resonance imaging (MRI) images (black arrows)

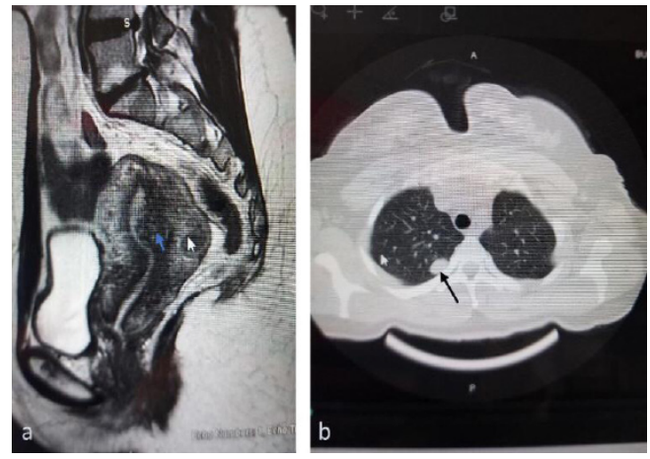

Figure 2. Magnetic resonance imaging (MRI) of the pelvis and chest computed tomography (CT). a) 25 mm type 3, 19 mm type 4 fibroids in the uterus (white and blue arrows) b) 17x12 mm nodule in the upper lobe of the right lung (black arrow)

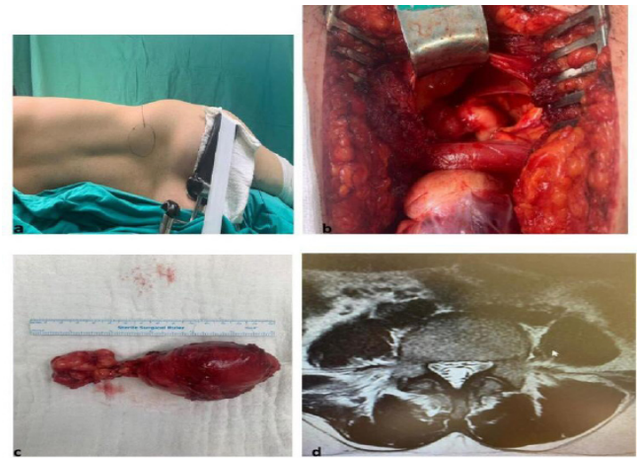

Figure 3. Symptomatic tumor located in the paraspinal lumbar muscle. a)Palpable well-circumscribed mass in the right side of the spine on lombarr vertebrae level. b) Intraoperative view of the mass. c) macroscopic view of the specimen. d) Postoperative lumbar Magnetic resonance imaging (MRI) image

where the mass was excised previously. Close surveillance of the patient continues. Written informed consent was obtained from the patient for participation and publication.

Discussion

Despite its metastatic potential, BML is a rare benign disease characterized by extrauterine multiple smooth muscle cell tumors, similar to uterine leiomyoma, seen mostly in women of reproductive age with a history of leiomyoma. The lungs are the most common site of involvement (79.5%). The majority of pulmonary BML cases present with multiple solid nodules (87%), they are often asymptomatic and found incidentally. Other less frequent metastasizing sites reported are lymph nodes, blood vessels, pelvis, muscular tissue, bone (skull, spine, femur), even pancreas and heart [2,3].

The pathologic mechanism of BML has not yet been elucidated. The fact that the majority of patients have a history of myomectomy or hysterectomy for leiomyoma suggests that there may be cardiovascular or lymphovascular spread of smooth muscle cells or direct peritoneal seeding due to surgical manipulation [3]. However, there are cases reported showing that BML can occur even without a history of gynecologic surgery [2]. Another theory relates to in situ hormone-sensitive proliferation of smooth muscle cells [4]. Karyotypic and molecular studies indicate that BML is clonally derived from benign-appearing uterine leiomyomas [5].

BML may show a range of clinical symptoms depending on the location of involvement and the number and size of the tumors. Although a detailed medical history and imaging studies are helpful in diagnosis, definitive diagnosis is dependent on pathologic examination. In pathologic evaluation, benign-appearing spindle-shaped cells reveal that the tumor is of a smooth muscle nature. Positive immunohistochemical staining for desmin, vimentin, SMA, ER, PR, negative for S-100 antigen, and a Ki-67 index less than 1%, signifying a low proliferate rate, confirm that benign mesenchymal tumors are similar to leiomyomas of uterine origin. Histopathologic features with low mitotic index (less than 5 mitoses per high-power field [hpf]), lack of nuclear atypia, absence of coagulative necrosis, and minimal vascularization differentiate the tumor from leiomyosarcoma [4].

In their review of 161 patients with BML, Barnas et al. reported that 128 of the patients had only lung metastases, and nine patients had lung and concomitant metastases. In 47.5% of the cases, the diagnosis was made when the patient was symptomatic, and the rest were found incidentally. The mean age at the first surgery was 38.5 years, the mean age at diagnosis was 47.3 years, and the average interval between the first surgery and diagnosis was 8.8 years [2]. Previously published data speculate that the estimated time from initial surgery to diagnosis of BML is 10 to 15 years [6]. Our case differs from other cases in the literature because it was diagnosed at the age of 30 years, only 1 year after the initial surgery, with a large size metastasis concurrent with lung metastasis.

Being positive for ER, frequently found in premenopausal patients, regression of lesions in cases of menopause and termination of pregnancy when endogenous estrogen decreases or when medical/surgical castration is performed, indicates that estrogen is the main factor in lesion progression [7].

Although there is no consensus on treatment, treatments aimed at reducing estrogen have been used in line with these findings. Close follow-up in young and asymptomatic patients, surgical removal of the metastatic tumor, medical treatment for suppressing endogenous estrogen in cases where surgery is not possible or not preferred have been suggested and performed for treatment. Medical castration with hormonal therapy such as GnRHa, progesterone antagonists (mifepristone), selective estrogen receptor modulators (SERMs), estrogen receptor antagonists (tamoxifen), or aromatase inhibitors (letrozole) could be recommended [1,7]. However, interestingly, it has been shown that lesions in postmenopausal patients may be resistant to hormonal therapy and may even progress [7]. There may be some other biologic controls or hormonal factors in the behavior of BML.

Nucci et al. [8] suggested that BML might originate from a biologically distinctive subset of uterine fibroids, in which chromosomal aberrations (19q and 22q terminal deletions) have been identified, found in approximately 3% of patients who have uterine leiomyoma. This result may help explain why every patient with leiomyoma does not develop BML. However, BML, which is a rare and complex condition, still has many unknowns. The overall incidence of BML after leiomyoma is unknown. The origin of individual differences in the response rate to medical treatment and progression pattern is unknown.

Conclusion

Our case, in which we are concerned that the increased oestrogen during pregnancy might continue to severely progress the existing myomas in the uterus and metastatic lesions, is important because it shows that this disease, which is stated to be effectively treated with surgical or medical castration, may still allow for a term pregnancy. Especially in young patients, after excluding the possibility of primary or concurrent malignancy of the tumor, untreated follow-up and determining the individual progression behavior of BML may be an appropriate approach.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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